Original Research Paper

Volume - 11 | Issue - 12 | December - 2021 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

Anaesthesiology

A COMPARATIVE STUDY OF THE EFFECTS OF INTRAVENOUS DEXMEDETOMIDINE AND INTRAVENOUS MAGNESIUM SULPHATE IN ATTENUATING THE ADVERSE CARDIOVASCULAR EFFECTS DUE TO LARYNGOSCOPY & ENDOTRACHEAL INTUBATION

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ABSTRACT **Introduction:** Laryngoscopy and tracheal intubation have profound influence on circulatory parameters and intracranial pressure. When planning the anesthetic induction these effects must be blunted as much as possible especially in the high risk population like patients with coronary artery disease, asthma, elevated intra-cranial pressure, cerebral aneurysm.

Material and Methods: This is prospective study conducted at Department of Anaesthesiology in a Tertiary care teaching hospital during the period of December 2018 to August 2019. Patients of both sexes in the age group of 18 to 50 years belong in to ASA grade-I & II posted for routine surgical procedures under different operating unit in whom general anaesthesia was maintained with endotracheal intubation. Patients with the above mentioned criteria were selected randomly from the indoor patients and were assessed pre-operatively and the suitable cases were prepared for the operation and the study.

Result: The patients were almost identical in relation to gender in the two groups although the number of female patients are more. Duration of anaesthesia is within the range of 30 -110 min. Duration of anaesthesia is compairable in both the group. There is significant rise ($p < 0.01$) in pulse rate in group-M patients at 1 min of intubation as compaired to group-D. The post intubation rise in pulse rate return back to normal within 5 min in group- D and within 10 min in group –M.

Conclusions: Dexmedetomidine, when compared to Magnesium Sulphate, provides light sedation while maintaining patient arousability, more analgesic sparing effects and greater reduction of heart rate. Hence. I.V premedication with dexmedetomidine in a dose of 1 mcg /kg may be recommended for patients at risk for complication arising from respiratory depression, analgesic drugs and tachycardia during perioperative period, despite its high cost.

KEYWORDS : Dexmedetomidine, Magnesium Sulphate, Laryngoscopy, Endotracheal intubation

INTRODUCTION:

Anaesthesia as a science has been well established and despite the safety of modem anaesthetic technique, catastrophes are occurring due to variety of factor to which the patient is subjected such as the patients with various anatomical and physiological variations and also the patients response to various techniques and drugs. [1]

Out of the various technique, general anaesthesia is the one, which is routinely and frequently practiced with the help of an anaesthetic machine (Boyles apparatus) delivering Oxygen & Nitrous oxide & inhalational anaesthetic agent and facilitating even to control the ventilation as per the need. [2]

To achieve this with the machine intubation of the trachea is inevitable to ensure a connecting channel for delivery of the anaesthetic vapour from the machine to the lungs. [3] Stress response to laryngoscopy and tracheal intubation have profound influence on circulatory parameters and intracranial pressure. When planning the anesthetic induction these effects must be blunted as much as possible especially in the high risk population like patients with coronary artery disease, asthma, elevated intra-cranial pressure, cerebral aneurysm etc [4]

Many attempts have been made to attenuate the pressure response i.e. deep anesthesia, topical anesthesia, use of ganglionic blockers, beta blockers, calcium channel blockers, lignocaine, clonidine etc. [5] Although these drugs did obtund the adverse cardio vascular effects due to Laryngoscopy and Intubation, none of them could fulfill the desired criteria of an ideal agent for complete attenuation. [6] An agent with quick onset, short duration without any active metabolite, having no deleterious effects or minimum drug interaction with high therapeutic index should be considered as an ideal one. [7]

Dexmedetomidine, an imidazole compound is a specific and selective $_2$ adreno receptor agonist. The mechanism of action is unique and differs from other sedative agents including clonidine. [8] The improved specificity of Dexmedetomidine for the $_2$A adreno receptor especially for the 2A sub-type of this receptor causes it to be an effective sedative, analgesic agent than clonidine. [9] Activation of pre-synaptic $_2$ receptor deactivates the sodium ion channel and calcium ion channel, hyperpolarizing the neuronal membrane and thus causes an inhibition of neuro-transmitter release. [10]

Magnesium sulphate has been used as anticonvulsant and antiarrhythmic agent. Recently, the importance of magnesium in anesthetic practice has been highlighted because of its antagonistic activity on Ca^{++} and NMDA receptor, inhibition of catecholamine release and vasodilatory effect of the ion [11]

Material And Methods

This is prospective study conducted at Department of Anaesthesiology in a Tertiary care teaching hospital during the period of December 2018 to August 2019. Patients of both sexes in the age group of 18 to 50 years belong in to ASA grade-I & II posted for routine surgical procedures under different operating unit in whom general anaesthesia was maintained with endotracheal intubation conducted at Department of Anaesthesiology, Tertiary care teaching hospital during the period of December 2018 to August 2019.

Patients with the above mentioned criteria were selected randomly from the indoor patients and were assessed pre-operatively and the suitable cases were prepared for the operation and the study.

Preoperative Preparation

After through assessment 120 patients were thus selected and the cases were prepared by overnight fasting and bed time oral tab Diazepam (10 Mg), and tab Ranitidine 150 mg day before operation and advised to take nothing orally on the day of operation.

Patients were divided into 2 demographically identical groups (in respect to age, weight, sex and race) comprising of 60 each at random and informed consent for the study was taken.

On the day of operation patients were brought to the preanaesthetic room at least 30 minutes earlier to operation (and usually the operation was carried out in the early hours of morning, around 9 A.M.) and a slow IV drip was started. The patients were divided into two groups.

Gr.D	Patients received IV Dexmedetomidine (1 mcg/Kg), 5 minute before induction
Gr. M	Patients received IV M_gSo_4(40 Mg/Kg), 5 minute before induction

RESULT

Table-I: Group Wise Distribution

Name of group	No. of patients	Name of study drugs
D	60	IV Dexmedetomidine
M	60	IV Magnesium Sulphate

Table-II: (Sex Wise Distribution Of Cases)

SEX	GROUP-D	GROUP-M
MALE (%)	10 (16.5)	12 (19.8)
FEMALE (%)	50 (83.5)	48 (79.2)

The patients were almost identical in relation to gender in the two groups although the number of female patients are more.

Table-III: (Age Wise Distribution Of Cases)

VARIABLE	GROUP-D	GROUP-M
AGE (YEARS) M±SD	41.73±8.17	39±10.498

Age of both the group were comparable

Table-IV: (Weight Wise Distribution Of Cases)

VARIABLE	GROUP-D	GROUP-M
WEIGHT(Kg) M±SD	52.47±6.14	53.5±6.27

All the cases are within the weight range of 35 -65 Kg

Table-V: (Duration Of Anaesthesia)

GROUP	NO.OF CASES	DURATION OF ANAESTHESIA IN MINS.	P*
D	60	82.1±22.02	0.9036
M	60	81.4±22.84	0.9036

P >0.05 Statistically not significant
Duration of anaesthesia is within the range of 30 -110 min
Duration of anaesthesia is compairable in both the group.

Table-VI: Perioperative Heart Rate (Mean±sd)

TIME	GROUP-D	GROUP-M
Preoperative	81±4.04	89.1±4.76
Pre intubation	82±4.29	83.1±4.12
1 min after intubation	86±4.6*	103.3±3.8**
2 min after intubation	84±4.4	98.4±3.7
5 min after intubation	82±4.0*	96.8±3.8*
10 min after intubation	80±4.6	90.6±3.4

There is significant rise ($p < 0.01$) in pulse rate in group-M patients at 1 min of intubation as compaired to group-D. The post intubation rise in pulse rate return back to normal within 5 min in group- D and within 10 min in group –M.

Table-VII: Systolic Blood Pressure In Mm Of Hg (Mean ± Sd)

TIME	GROUP-D	GROUP-M
Preoperative	122±4.77	120.6±3.41
Pre intubation	118.6±3.66	122.01±4.63
1 min after intubation	127.2±5.6	130.9±4.9
2 min after intubation	123.4±3.2	128.4±4.0
5 min after intubation	122.6±4.31	127.0±4.0
10 min after intubation	120.9±4.39	125.7±3.49
15 min after intubation		

This table indicates that the post-intubation rise in systolic blood pressure has returned back to almost pre-intubation value after 5 min in group- D and within 10 min in group –M.

Table –VIII: Diastolic Blood Pressure In Mm Of Hg (Mean ± Sd)

TIME	GROUP-D	GROUP-M
Preoperative	81.2±4.51	84.6±3.87
Pre intubation	79.6±3.92	85.3±4.68
1 min after intubation	81.5±5.1	92.3±3.66**
2 min after intubation	80.9±5.0	90.2±3.0
5 min after intubation	80.9±4.39	88.1±3.61
10 min after intubation	80.4±4.0	86±3.57

** $p < 0.01$ statistically significant

In group-D there is no significant change in DBP in response to intubation. In group-M there is rise in DBP after 1 min which reverted back to preintubation value after 10 min of intubation.

Table –IX: Mean Arterial Pressure In Mm Of Hg (Mean ± Sd)

TIME	GROUP-D	GROUP-M
Preoperative	93.87±6.14	95.2±3.4
Pre intubation	92.6±3.7	98.5±3.94
1 min after intubation	96.7±5.25	103.1±3.8**
2 min after intubation	95.4±5.03	102.1±3.6
5 min after intubation	94.8±4.34	101.0±3.64
10 min after intubation	93.87±4.1	97.6±5.2

** $p < 0.01$ statistically significant

In group-D there is no significant change in MAP in response to intubation. In group-M there is rise in MAP after 1 min which reverted back to preintubation value after 10 min of intubation.

None of the patients among two groups developed any ECG abnormalities.

There were no significant difference in pre and intra operative SpO_2 values.

DISCUSSION:

Dexmedetomidine, an imidazole compound is a specific and selective $_2$ adreno receptor agonist. The mechanism of action is unique and differs from other sedative agents including clonidine. The improved specificity of Dexmedetomidine for the $_2$A adreno receptor causes it to be an effective sedative, analgesic, anxiolytic and sympatholytic agent. [12] Activation of post-synaptic $_2$ receptor deactivates the sodium ion channel and calcium ion channel, hyperpolarizing the neuronal membrane, thus causing an inhibition of neuro-transmitter release and augmentation of vagal activity. They also inhibit release of catecholamines from sympathetic nerve terminal by augmentation of vasoconstrictive effect, and attenuate the pressore response during laryngoscopy and surgery.[13]

Magnesium sulphate has been used as anticonvulsant and antiarrhythmic agent. Recently, the importance of magnesium in anesthetic practice has been highlighted because of its antagonistic activity on Ca^{++} and NMDA receptor, inhibition of catecholamine release and vasodilatory effect of the ion. Thus we conducted this prospective randomized study in an attempt to examine whether Dexmedetomidine or Magnesium sulphate which attenuate the pressure response during laryngoscopy and surgery better. [14]

The result of the study was discussed with observation of other workers in this field of work, taking steps to account for difference as far as possible. The discussion of the various aspect of this study are as follows. In group D & group M, the mean age of patient are 41.7 &, 39 respectively. Almost equal age wise distribution were observed in all the two groups (Table-III). In group D and Group M the M : F ratio was 10:50. Almost equal sex wise distribution were observed in two groups (Table-II). The weight of the patients have been considered for the purpose of dosage calculation of anasthetic drugs used. Patient in the two group did not show any significant variation (Table-IV). The patients were identical in relation to sex, age and weight in all the two groups.

Table VI shows the variation in mean pulse rate at 1, 3, 5 & 10min interval after intubation in relation to preintubation value. There was rise in pulse rate in both the groups at 1 min of intubation. But the rise was significant ($p < 0.01$) in group-M patients as compared to group-D. The pulse rate in both the groups decreased at 2 min of intubation. But the decrease was more in group-D patients as compared to group-M. The pulse rate in group-D return back to normal level and remained quite stable there after through out the intra operative period.

In group- M though the rise at 1 min was reduced, it did not come down to normal level, but the rise in pulse rate was no more significant. Group-D patients are already stable at the normal level from 5 min onwards. In group- M patients there was a further fall in mean pulse rate and return back to normal level and maintained through out the intra operative period.

Moreover HR in group D was lower than Group M. The trend of change in HR was similar in the test group though more magnified in group M. The rise in HR in response to intubation and extubation was suppressed in both the study group, though it might reflect a lower pre –induction and pre extubation HR in group-D.

Both magnesium sulfate and dexmedetomidine decreased HR below baseline similar to the study of Aho M, et al 1991. [16]Dexmedetomidine

induced a statically significant with the finding of Jaakola et al [17], they showed that following dexmedetomidine, there was a 16%-20% decrease from baseline of HR. Lethinen AM, et al 1991[18] in their study noted that the HR response was significantly less with dexmedetomidine versus fentanyl.

Table IX shows the variation in mean arterial pressure at 1, 3, 5 & 10 min interval after intubation in relation to preintubation value. The pattern of mean arterial pressure represents the presentation of both mean systolic blood pressure and mean diastolic blood pressure. There was no significant change in mean arterial pressure in group D. However, in group-M there was a significant increase in mean arterial pressure. The mean arterial pressure in both the groups decreased at 2 min of intubation. But the decrease was more in group-D patients as compared to group-M. The mean arterial pressure in group-D return back to normal level and remained quite stable thereafter throughout the intra operative period.

In group- M though the rise at 1 min was attenuated but it did not come down to normal level, the rise in mean arterial pressure was no more significant. In group-D patients, there was no change in mean arterial pressure and patients are already stable at the normal level from 5 min onwards.

In group- M patients there was a further fall in mean arterial pressure pulse and return back to normal level and maintained throughout the intra operative period.

The MAP of group D was almost always lower than in group M. The trend of rise in MAP was more magnified in group M and the fall in MAP was more mangified in the Group D. The haemodynamic effect of a bolous dose of dexmedetomidine in humans have shown a biphasic response but here it was not produced because of low dose and giving loding dose over 5 minutes as evaluated by the study of Fraser GL et al 2005.[19]

The total amount of rescue tramadol required was less in patient premedicated with dexmedetomidine. Similar analgesic effects of dexmedetomidine have been demonstrated by Umlugenc H el al 2005. [20] Dexmedetomidine(1Mcg/kg) admnistered 5 minutes prior to anesthetic induction reduced morphine PCA requrements following abdominal surgery in adults by 28% during the first 24 hours postoperatively. Similar findigs were reported by Arain et al, [21] who reported dexmedetomidine required less morphine in the PACU (4.5 + 6.8 vs 9.2 = 5.2 mg). after 60 minutes in the PACU, 6 of 17 patients who received dexmedetomidine requred morphine versus 15 of 17 in the control group.

The incidence of bradycardia and hypotension occurred in the test group-D, as shown by Erkola 0 et al 1994. [22]They concluded that in patients undergoing abdominal hysterectomy premedicated with dexmedetomidine, bradycardia was more common than in those who were premedicated with midazolam.

The magnasium sulfate pretreated group my study report corroborate well with findings of games M.F.M and others (1989) [23] ; R.W. Allen, P.C Uys, and other (1991). [103] They have found that magnesium sulphate pretreatment could attenuate the post intubation rise in heart rate and blood pressure significantly as compared to control group.

Endotracheal anaesthesia was conceived in the last quarter of 19th century. Ever since its inception, it has been known that the passage of endotracheal tube is accompanied with certain changes in cardio-vascular system.

Laryngoscopy and intubation cause hypertension, tachycardia, arrhythmias and attenuation of these changes is important and more so in patients with coronary artery disease. In response to laryngoscopy and intubation, heart rate, systolic blood pressure and mean arterial pressure increases significantly.

After starting a slow intervenous drip all the patients were brought to the OT and were given IV Glycopyrrolate and Pentazocine as premedication. The patients were induced with Thiopentone and intubation was done with vecuronium bromide. The patient were maintained with O_2:N_2O: 50:50 (2:2) in Bain coaxial circuit and IPPV, and intermittent dose of inj. vecuronium when required. Reveresal was done with Neostigmine and glycopyrrolate.

CONCLUSIONS

Dexmedetomidine, when compared to Magnesium Sulphate, provides light sedation while maintaining patient arousability, more analgesic sparing effects and greater reduction of heart rate. Hence. I.V premedication with dexmedetomidine in a dose of 1 mcg /kg may be recommended for patients at risk for complication arising from respiratory depression, analgesic drugs and tachycardia during perioperative period, despite its high cost. So it may be concluded that clinicians desiring to provide protection for their patients against intubation related changes in heart rate and blood pressure should utilize dexmedetomidine in a dose of 1 mcg /kg 5 min before induction.

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